

SEQUENCE LISTING

<110> Kim, Jospeh L
Morgenstern, Kurt A
Caron, Paul R
Lin, Chao
Vertex Pharmaceuticals Inc.

<120> CRYSTALS OF HEPATITIS C VIRUS HELICASE OR FRAGMENTS THEREOF
COMPRISING A HELICASE BINDING POCKET

<130> Sequence listing for VPI/97-101 CIP CON

<140>

<141>

<150> PCT/US98/16879

<151> 1998-08-13

<160> 4

<170> PatentIn Ver. 2.0

<210> 1

<211> 1932

<212> DNA

<213> Hepatitis C virus

<220>

<221> CDS

<222> (4)...(1896)

<223> Full length HCV NS3 coding sequence

<220>

<221> misc_feature

<220>

<221> misc_feature

<222> (504)..(1896)

<223> Helicase domain

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atg gcg ccc atc acg gcg tac gcc cag cag acg aga ggc aag ctt ggg 48

Ala Pro Ile Thr Ala Tyr Ala Gln Gln Thr Arg Gly Lys Leu Gly

1 5 10 15

tgt ata atc acc agc ctg act ggc cgg gac aaa aac caa gtg gag ggt 96

Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly

20 25 30

gag gtc cag atc gtg tca act gct acc caa acc ttc ctg gca acg tgc 144

Glu Val Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Cys

35 40 45

atc aat ggg gta tgc tgg act gtc tac cac ggg gcc gga acg agg acc 192

Ile Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr

50 55 60

atc gca tca ccc aag ggt cct gtc atc cag atg tat acc aat gtg gac 240

Ile Ala Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp

| | | | |
|---|-----|-----|----|
| 65 | 70 | 75 | |
| caa gac ctt gtg ggc tgg ccc gct cct caa ggt tcc cgc tca ttg aca 288 | | | |
| Gln Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr | | | |
| 80 | 85 | 90 | 95 |
| ccc tgc acc tgc ggc tcc tcg gac ctt tac ctg gtt acg agg cac gcc 336 | | | |
| Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala | | | |
| 100 | 105 | 110 | |
| gac gtc atc ccg gtt cgc cgt cgc ggt gat agc cgt ggt agc ctg ctg 384 | | | |
| Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu | | | |
| 115 | 120 | 125 | |
| tct ccg cgt ccg att tcc tac ctg aaa ggc tcc tcg ggg ggt ccg ctg 432 | | | |
| Ser Pro Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu | | | |
| 130 | 135 | 140 | |
| ttg tgc ccc gcg gga cac gcc gtg ggc cta ttc agg gcc gcg gtg tgc 480 | | | |
| Leu Cys Pro Ala Gly His Ala Val Gly Leu Phe Arg Ala Ala Val Cys | | | |
| 145 | 150 | 155 | |
| acc cgt gga gtg gcc aag gcg gtg gac ttt atc cct gtg gag aac ctg 528 | | | |
| Thr Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Asn Leu | | | |

| | | | |
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| 160 | 165 | 170 | 175 |
| gag acc acc atg cgt tcc ccg gtg ttc acg gac aac tcc tct cca cca 576 | | | |
| Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro | | | |
| 180 | 185 | 190 | |
| gct gtt ccc cag agc ttc cag gtg gcc cac ctg cat gct ccc acc ggc 624 | | | |
| Ala Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly | | | |
| 195 | 200 | 205 | |
| agt ggt aag agc acc aag gtc ccg gct gcg tac gca gcc cag ggc tac 672 | | | |
| Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr | | | |
| 210 | 215 | 220 | |
| aag gtg ttg gtg ctc aac ccc tct gtt gct gca acg ctg ggc ttt ggt 720 | | | |
| Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly | | | |
| 225 | 230 | 235 | |
| gct tac atg tcc aag gcc cat ggg gtc gat cct aat atc cgc acc ggt 768 | | | |
| Ala Tyr Met Ser Lys Ala His Gly Val Asp Pro Asn Ile Arg Thr Gly | | | |
| 240 | 245 | 250 | 255 |
| gtg cgt aca att acc act ggc agc ccc atc acg tac tcc acc tac ggc 816 | | | |

Val Arg Thr Ile Thr Thr Gly Ser Pro Ile Thr Tyr Ser Thr Tyr Gly

260

265

270

aag ttc ctt gcc gac ggc ggg tgc tca ggt ggc gct tat gat atc atc 864

Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile

275

280

285

att tgt gac gag tgc cac tcc acg gat gcc aca tcc atc ttg ggc atc 912

Ile Cys Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile

290

295

300

ggc act gtc ctt gac caa gca gag act gcg ggg gcg aga ttg gtt gtg 960

Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val

305

310

315

ctc gcc act gct acc cct ccg ggc tcc gtc acg gta ccg cat cct aac 1008

Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn

320

325

330

335

atc gag gag gtt gct ctg tcc acc acc gga gag atc cct ttc tac ggc 1056

Ile Glu Glu Val Ala Leu Ser Thr Thr Gly Glu Ile Pro Phe Tyr Gly

340

345

350

aag gct atc ccc ctc gag gtg atc aag ggc ggc cgt cat ctc atc ttc 1104

Lys Ala Ile Pro Leu Glu Val Ile Lys Gly Gly Arg His Leu Ile Phe

355

360

365

tgt cac tca aag aag aag tgc gac gag ctc gcc gcg aag ctg gtc gca 1152

Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala

370

375

380

ttg ggc atc aat gcc gtg gcc tac tac cgc gga ctt gac gtg tct gtc 1200

Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val

385

390

395

atc ccg acc agc ggc gat gtt gtc gtc gtg gcg acc gat gct ctc atg 1248

Ile Pro Thr Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met

400

405

410

415

act ggc ttt acc ggc gac ttc gac tct gtg ata gac tgc aac acg tgt 1296

Thr Gly Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys

420

425

430

gtc act cag aca gtc gat ttc agc ctt gac cct acc ttt acc att gag 1344

Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu

435

440

445

aca acc acg ctc ccc cag gat gct gtc tcc agg act cag cgc cgt ggt 1392

Thr Thr Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly

450

455

460

cgt acc ggc cgt ggg aag cca ggc atc tac aga ttt gtg gca ccg ggg 1440

Arg Thr Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly

465

470

475

gag cgc ccc tcc ggc atg ttc gac tcg tcc gtc ctc tgt gag tgc tat 1488

Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr

480

485

490

495

gac gcg ggc tgt gct tgg tat gag ctc acg ccg gcg gag act aca gtt 1536

Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val

500

505

510

cgt ctg cgc gcg tac atg aac acc ccg ggg ctt ccc gtg tgc cag gac 1584

Arg Leu Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp

515

520

525

cat ctt gaa ttt tgg gag ggc gtc ttt acg ggc ctc acc cat atc gat 1632

His Leu Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp

530

535

540

gcc cac ttt ctg tcc cag aca aag cag agt ggg gag aac ttt cct tac 1680

Ala His Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Phe Pro Tyr

545

550

555

ctg gta gcg tac caa gcc acc gtg tgc gct cgt gcg caa gcc cct ccg 1728

Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro

560

565

570

575

cca tcg tgg gac cag atg tgg aag tgt ttg atc cgc ctt aaa ccc acc 1776

Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr

580

585

590

ctc cat ggg cca aca ccg ctc ctg tac cgt ctg ggc gct gtt cag aat 1824

Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn

595

600

605

gaa gtc acc ctg acg cac cca atc acc aaa tac atc atg aca tgc atg 1872

Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Thr Cys Met

610

615

620

tcg gcc gac ctg gag gtc gtc acg ggatctggct cgcacatcatca tcatcatcac 1926

Ser Ala Asp Leu Glu Val Val Thr

625

630

taatag

1932

<210> 2

<211> 631

<212> PRT

<213> Hepatitis C virus

<400> 2

Ala Pro Ile Thr Ala Tyr Ala Gln Gln Thr Arg Gly Lys Leu Gly Cys

1 5 10 15

Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu

20 25 30

Val Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Cys Ile

35 40 45

Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile

50 55 60

Ala Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp Gln

65 70 75 80

Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro

85 90 95

Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp

100 105 110

Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser

| | | |
|---|-----|-----|
| 115 | 120 | 125 |
| Pro Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu | | |
| 130 | 135 | 140 |
| Cys Pro Ala Gly His Ala Val Gly Leu Phe Arg Ala Ala Val Cys Thr | | |
| 145 | 150 | 155 |
| Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Asn Leu Glu | | |
| 165 | 170 | 175 |
| Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro Ala | | |
| 180 | 185 | 190 |
| Val Pro Gln Ser Phe Gln Val Ala His Leu His Ala Pro Thr Gly Ser | | |
| 195 | 200 | 205 |
| Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr Lys | | |
| 210 | 215 | 220 |
| Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly Ala | | |
| 225 | 230 | 235 |
| Tyr Met Ser Lys Ala His Gly Val Asp Pro Asn Ile Arg Thr Gly Val | | |
| 245 | 250 | 255 |
| Arg Thr Ile Thr Thr Gly Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys | | |
| 260 | 265 | 270 |
| Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile | | |
| 275 | 280 | 285 |

Cys Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly
290 295 300

Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu
305 310 315 320

Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn Ile
325 330 335

Glu Glu Val Ala Leu Ser Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys
340 345 350

Ala Ile Pro Leu Glu Val Ile Lys Gly Gly Arg His Leu Ile Phe Cys
355 360 365

His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala Leu
370 375 380

Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile
385 390 395 400

Pro Thr Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met Thr
405 410 415

Gly Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val
420 425 430

Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr
435 440 445

Thr Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly Arg

| | | |
|---|-----|---------|
| 450 | 455 | 460 |
| Thr Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu | | |
| 465 | 470 | 475 480 |
| Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp | | |
| 485 | 490 | 495 |
| Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg | | |
| 500 | 505 | 510 |
| Leu Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His | | |
| 515 | 520 | 525 |
| Leu Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp Ala | | |
| 530 | 535 | 540 |
| His Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Phe Pro Tyr Leu | | |
| 545 | 550 | 555 560 |
| Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro | | |
| 565 | 570 | 575 |
| Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu | | |
| 580 | 585 | 590 |
| His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu | | |
| 595 | 600 | 605 |
| Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Thr Cys Met Ser | | |
| 610 | 615 | 620 |
| Ala Asp Leu Glu Val Val Thr | | |

625

630

<210> 3

<211> 8157

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Genetically
engineered plasmid containing full-length HCV NS3
coding sequence

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gagaggcaag cttgggtgta taatcaccag cctgactggc cgggacaaaa accaagtgga 180

gggtgaggtc cagatcgtgt caactgctac ccaaaccctc ctggcaacgt gcatcaatgg 240

ggtatgctgg actgtctacc acggggccgg aacgaggacc atcgcatcac ccaagggtcc 300

tgtcatccag atgtatacca atgtggacca agaccttggt ggctggcccg ctctcaagg 360

ttccccgtca ttgacaccct gcacctgagg ctctcggac ctttacctgg ttacgaggca 420

cgccgacgtc atccccgttc gccgtcggg tgatagccgt ggtagcctgc tgtctccgag 480

tccgatttcc tacctgaaag gctcctggg gggtcgctg ttgtgcccc cgggacacgc 540

cgtggggccta ttcaggggccg cgggtgacac ccgtggagtg gccaaaggcg tggactttat 600

ccctgtggag aacctggaga ccaccatgag tccccggtg ttacaggaca actcctctcc 660

accagctgtt cccagagct tccaggtggc ccacctgcat gctcccaccg gcagtggtaa 720

gagcaccaag gtcccggtg cgtacgcagc ccagggtac aagggtgttg tgctcaaccc 780

ctctgttgct gcaacgctgg gctttggtg ttacatgtcc aaggcccatg gggtcgatcc 840

taatatccgc accggtgtg gtacaattac cactggcagc cccatcacgt actccaccta 900

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at t t t t g g g a g g g c g t c t t t a c g g g c c t c a c c c a t a t c g a t g c c c a c t t t c t g t c c c a g a c 1740

a a a g c a g a g t g g g g a g a a c t t t c c t t a c c t g g t a g c g t a c c a a g c c a c c g t g t g c g c t c g 1800

t g c g c a a g c c c c t c c g c c a t c g t g g g a c c a g a t g t g g a a g t g t t t g a t c c g c c t t a a a c c 1860

c a c c c t c c a t g g g c c a a c a c c g t c c t g t a c c g t c t g g g c g c t g t t c a g a t g a a g t c a c 1920

c c t g a c g c a c c c a a t c a c c a a a t a c a t c a t g a c a t g c a t g t c g g c c g a c c t g g a g g t c g t 1980

c a c g g g a t c t g g c t c g c a t c a t c a t c a t c a t c a t a a t a g a a t t c g g a t c c g g t g c t a a 2040

c a a a g c c c g a a a g g a a g c t g a g t t g g c t g c t g c c a c c g c t g a g c a a t a a c t a g c a t a a c c 2100

c c t t g g g g c c t c t a a a c g g g t c t t g a g g g g t t t t t t g c t g a a a g g a g g a a c t a t a t c c g g 2160

a t a t c c c g c a a g a g g c c c g g c a g t a c c g g c a t a a c c a a g c c t a t g c c t a c a g c a t c c a g g 2220

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